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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/744,675	01/29/2001	Edward L. Squires	XY-EQUINE3-U	3456
33549	7590	07/13/2004	EXAMINER MYERS, CARLA J	
SANTANGELO LAW OFFICES, P.C. 125 SOUTH HOWES, THIRD FLOOR FORT COLLINS, CO 80521			ART UNIT	PAPER NUMBER

1634

DATE MAILED: 07/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/744,675

Applicant(s)

SQUIRES ET AL.

Examiner

Carla Myers

Art Unit

1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 April 2004 and 27 May 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 45-51 and 136-145 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 45-51 and 136-145 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on April 9, 2004 has been entered. This action is made non-final.

THE FOLLOWING CONSTITUTE NEW/MODIFIED GROUNDS OF
OBJECTION/REJECTION

Objections

2. The claims are objected to because of the following informalities:
In claims 137 and 145, "and1ml" should read "and 1ml".

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

Art Unit: 1634

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 45-47 and 49-51, 136-140, and 142-145 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rens (U.S. Patent No. 5,985,216) in view of Wilhelm (Cryobiology (1996) 33:320-329) and further in view of Rath (Theriogenology. April 1997, 795-800; cited in the IDS) .

Rens teaches a method of high speed flow cytometry for sorting sperm. In the method of Rens (see columns 4-6), a sample of sperm is obtained from a male mammal, the sperm is stained with Hoeschst 33342 dye in order to distinguish between viable and nonviable sperm (column 5, lines 4-10), the sperm are sorted in a high speed flow cytometer using a nozzle that forms a stable droplet containing each individual sperm cell (column 2, lines 23-32), the sperm are sorted according to their sex characteristics and isolated populations of X- and Y-chromosome bearing sperm are collected. Approximately 50% of the sperm were viable and the sorting was performed at sampling rates of 500 sperm/sec and 2000 sperm/sec (see column 6). Further, the nozzle allowed for sample rates up to at least 15,000 sperm/sec (column 4, lines 29-31). Rens exemplifies using the claimed sorting method using rabbit, bull, mouse and human sperm (columns 4-7) and states that the sorting method can be used with any

Art Unit: 1634

mammalian sperm (column 4, lines 38-42). Rens does not specifically exemplify applying the sorting method to equine sperm.

However, Wilhelm teaches the use of equine sperm for the purpose of artificial insemination. It would have been obvious to one of ordinary skill in the art at the time the invention was made to have applied the method of Rens to the sorting of equine sperm in order to have provided an effective means for distinguishing between and collecting populations of X- and Y-chromosome bearing sperm useful for artificially inseminating equine.

Secondly, Rens does not specify the solution into which the sperm cells are collected and thereby does not teach collecting the sorted sperm in a skim milk solution. However, Rath (page 796) teaches collecting sex-sorted sperm into a collection media composed of TEST extender containing 2% hen egg yolk. Thus, Rath teaches the concept of collecting sperm sorted cells into a sperm extender medium. Wilhelm teaches extending equine sperm in skim milk solution containing 2% egg yolk by volume (page 322; referred to therein as SMEY). Wilhelm teaches that SMEY extender effectively preserves equine sperm during freezing and thawing and teaches that egg yolk and skim milk may contain components which protect spermatozoa membranes (page 326).

Accordingly, in view of the teachings of Rath and Wilhelm, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have further modified the method of Rens so as to have collected the equine sperm in the SMEY extender solution of skim milk and egg yolk in order to have sorted the sperm

Art Unit: 1634

into a medium that helped to preserve the sperm and/or which could be used for subsequently freezing and then thawing the sorted equine sperm. Specifically, Rath teaches that the sorted sperm are collected into a tube containing sperm extender and it would have been obvious to the ordinary artisan that alternative extenders that were known in art to be effective for preserving equine sperm, such as the skim milk extender of Wilhelm, could be present in the collection tube in order to ensure the proper collection of the sperm.

With respect to claims 47 and 140, the recitation of "about four percent egg yolk" is considered to encompass 2% egg yolk. Furthermore, it would have been well within the skill of the art at the time the invention was made to have modified the concentration of egg yolk in the extender solution in order to have provided the most effective concentration of egg yolk depending on the other reagents present in the extender solution.

With respect to claims 51 and 143, Rens does not specify the pressure used to operate the high speed cell sorter. However, methods for sorting equine sperm using high speed cell sorters were well known in the art at the time the invention was made. To determine the optimum conditions for performing a method step is well within the skill of the art. As discussed in MPEP 2144.05(b), "(w)here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. *In re Aller*, 220 F.2d 454, 105 USPQ 233, 235 (CCPA 1955).

Art Unit: 1634

With respect to claims 136, 137, 144 and 145, Rens teaches that 4 to 5 million sorted sperm were used to inseminate dairy cows, but does not teach the quantity and volume of sperm in equine artificial insemination samples. Additionally, Rath (page 796) teaches the use of .2 million sorted porcine spermatozoa per oviduct and teaches resuspending sorted porcine sperm in a solution having a volume of .2 ml. Rath teaches that approximately 3.5 to 4×10^5 sperm cells were sorted into each tube. Since the parameters which effect artificial insemination of equine were known in the art at the time the invention was made, it would have been obvious to one of ordinary skill in the art and well within the skill of the art to have selected an optimum quantity of sperm, wherein said quantity would be less than 25 million and to have selected the optimum volume for the artificial insemination sample, so as to have provided the most effective sample for inseminating equine while keeping the number of sperm to be used for insemination at the lowest possible number given the constraints on how many sperm could be sorted per day and the cost of sorting. Additionally, the ordinary artisan would have recognized that the quantity of sperm and the volume of the sperm sample could be modified in order to have provided the most appropriate sperm sample depending on how the sample would be used – i.e., depending on the amount of sperm present in the original sample, whether the samples would be frozen prior to use, the number of samples to be used for insemination, and the type of insemination technique. Accordingly, to have generated sorted sperm samples containing less than 5 or 25 million sperm or to have generated sorted sperm samples in a volume of .2 or 1 ml would have been obvious to one of ordinary skill in the art because the ordinary artisan

Art Unit: 1634

would have recognized that the quantity of sperm and the volume of sample should be varied depending on how the sperm sample was to be further processed and / or used.

4. Claims 48 and 141 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rens in view of Wilhelm and Rath and further in view of Catt (cited in the IDS of January 29, 2001).

The teachings of Rens, Wilhelm and Rath are presented above. The combined references do not teach establishing a sheath fluid which contains a HEPES buffered medium. Catt teaches that semen may be diluted in a HEPES-buffered SOF (synthetic oviduct fluid) medium and that such a fluid is suitable for maintaining the viability of spermatozoa (see, e.g., page 252 and 257). Catt also teaches that it is beneficial to sort into a medium containing a cushioning of seminal plasma to increase the viability and motility of sperm. Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have further modified the method of Rens in view of Wilhelm so as to have used a HEPES-buffered medium for establishing a sheath fluid because Catt teaches that this is a suitable dilution medium for sperm and thereby using HEPES-buffered medium as the sheath fluid would have achieved the benefit of ensuring the viability and motility of the sperm.

5. Claims 45-51 and 136-145 are rejected under 35 U.S.C. 103(a) as being unpatentable over Seidel (U.S. Patent No. 6,149,867) in view of Wilhelm (Cryobiology (1996) 33:320-329) and further in view of Rath (Theriogenology. April 1997, 795-800; cited in the IDS).

It is noted that the '867 patent and the present application share a common inventor and assignee. However, the inventorship and assignee of the '867 patent is distinct from that of the present application.

Seidel teaches a method of high speed flow cytometry for sorting equine sperm. The method of Seidel comprises obtaining a sample of sperm from a male mammal, staining the sperm in order to distinguish between viable and nonviable sperm, sorting the speed using a high speed flow cytometer having a nozzle that forms a stable droplet containing each individual sperm cell wherein the sperm are sorted according to their sex characteristics and isolating populations of X- and Y-chromosome bearing sperm are collected (see column 6). Seidel (column 7) teaches sorting at rates of greater than 500 sorts per second and up to 1000 to 1200 sorts per second. The reference also teaches operating the flow cytometer at pressures of about 50 lbs per square inch (column 7). Seidel teaches that when sorting equine sperm, the preferred sheath fluid contains HEPES buffer (column 9).

Seidel teaches that "it has been known to place an initial collector fluid (17) in the bottom of the container to collect the cells so that they do not hit the bottom of the container" (column 10). Seidel states that the collector fluid "may serve to minimize chemical stresses upon the cells. In one regard, since it may be important to provide a nutrient to the cells both before and after sorting, the collector fluid (17) may be selected so as to provide a coordinated level of nutrient so that the levels are balanced both before and after sorting" (column 10). The reference teaches that an egg yolk solution may be used as the collection fluid and that the collection fluid may be chosen so that it

Art Unit: 1634

is similar to the starting fluid environment or any other fluid environment used in the method (column 11). It is also stated that that the levels of egg yolk may be varied "as those skilled in the art readily understand" (column 11).

Seidel does not specifically teach using a collection fluid that contains skim milk. However, Rath (page 796) teaches collecting sex-sorted sperm into a collection media composed of TEST extender containing 2% hen egg yolk. Thus, Rath teaches the concept of collecting sperm sorted cells into a sperm extender medium. Wilhelm teaches extending equine sperm in skim milk solution containing 2% egg yolk by volume (page 322; referred to therein as SMEY). Wilhelm teaches that SMEY extender effectively preserves equine sperm during freezing and thawing and teaches that egg yolk and skim milk may contain components which protect spermatozoa membranes (page 326).

Accordingly, in view of the teachings of Rath and Wilhelm, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Seidel so as to have collected the equine sperm in the SMEY extender solution of skim milk and egg yolk in order to have sorted the sperm into a medium that helped to preserve the sperm and/or which could be used for subsequently freezing and then thawing the sorted equine sperm. Specifically, Rath teaches that the sorted sperm are collected into a tube containing sperm extender and it would have been obvious to the ordinary artisan that alternative extenders that were known in art to be effective for preserving equine sperm, such as the skim milk extender of Wilhelm,

Art Unit: 1634

could be present in the collection tube in order to ensure the proper collection of the sperm.

With respect to claims 47 and 140, the recitation of "about four percent egg yolk" is considered to encompass 2% egg yolk. Furthermore, as taught by Seidel, it would have been well within the skill of the art at the time the invention was made to have modified the concentration of egg yolk in the extender solution in order to have provided the most effective concentration of egg yolk depending on the other reagents present in the extender solution.

With respect to claims 136, 137, 144 and 145, Seidel (column 12) teaches using a low dose of sperm for artificial insemination and teaches concentrating bovine sperm to a level of 3-5 million sperm cells per ml (column 13), but does not teach the quantity and volume of sperm in an equine artificial insemination sample. Additionally, Rath (page 796) teaches the use of .2 million sorted porcine spermatozoa per oviduct and teaches resuspending sorted porcine sperm in a solution having a volume of .2 ml. Rath teaches that approximately 3.5 to 4×10^5 sperm cells were sorted into each tube. Since the parameters which effect artificial insemination of equine were known in the art at the time the invention was made, it would have been obvious to one of ordinary skill in the art and well within the skill of the art to have selected an optimum quantity of sperm, wherein said quantity would be less than 25 million and to have selected the optimum volume for the artificial insemination sample, so as to have provided the most effective sample for inseminating equine while keeping the number of sperm to be used for insemination at the lowest possible number given the constraints on how many

Art Unit: 1634

sperm could be sorted per day and the cost of sorting. Additionally, the ordinary artisan would have recognized that the quantity of sperm and the volume of the sperm sample could be modified in order to have provided the most appropriate sperm sample depending on how the sample would be used – i.e., depending on the amount of sperm present in the original sample, whether the samples would be frozen prior to use, the number of samples to be used for insemination, and the type of insemination technique. Accordingly, to have generated sorted sperm samples containing less than 5 or 25 million sperm or to have generated sorted sperm samples in a volume of .2 or 1 ml would have been obvious to one of ordinary skill in the art because the ordinary artisan would have recognized that the quantity of sperm and the volume of sample should be varied depending on how the sperm sample was to be further processed and / or used.

6. RESPONSE TO ARGUMENTS:

In the response filed April 9, 2004, Applicants traversed the previous grounds of rejection by arguing that Wilhelm teaches using a skim milk solution as an extender for freezing and thawing sorted sperm, but does not teach collecting the sorted sperm into a skim milk solution. It is stated that the teachings of the reference are different from those of the present claims and that the references do not suggest using the skim milk solution as a collection fluid. Applicant's arguments have been fully considered but are not persuasive to overcome the present grounds of rejection. While Rens does not specifically discuss the collection fluid that is used to collect the sorted sperm, Rath does teach that the sorted sperm should be deposited into a tube that contains an extender. Rath exemplifies collecting porcine sorted sperm in a TEST-egg yolk extender

Art Unit: 1634

solution. The ordinary artisan would have recognized that alternative extender solutions could also be used to collect the sorted sperm. Wilhelm teaches such a solution for use with equine sperm. Specifically, Wilhelm teaches using the extender SMEY, which contains skim milk and egg yolk, as an extender. Wilhelm teaches that SMEY provides an effective fluid for protecting sperm. Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have collected the sorted sperm in the SMEY solution of Wilhelm because this would have provided an effective medium for protecting the sorted sperm and would have provided a medium that could be used for subsequent freezing of the sperm.

Applicants further argue that the combined references do teach operating the flow cytometer at a pressure of 50 psi and the combined references do not suggest using separation rates of at least 900 viable equine sperm cells per second. Applicants state that the results obtained under the stated conditions are unexpected. However, Applicants have not provided any factual evidence to support their contention of unexpected results. Applicants have not shown improved and unexpected results under all conditions, using any type of separation device, at pressures of 50 psi and at all pressures above 50 psi. Nor have applicants shown improved and unexpected results under all conditions and using any type of separation device at sort rates at 900 viable sorted equine sperm cells per second and at all sort rates above 900 viable sorted sperm cells per second. Applicants further state that "Contrary to the assertion made in the Office Action, it is incumbent upon the Office to provide evidence supporting its allegation that the stated values are in fact obvious." However, it is maintained that

Art Unit: 1634

optimization of the flow rates and pressure would have been well within the skill of the art at the time the invention was made given the fact that the prior art recognized how the parameters of pressure and sort rates effected the sorting process and the viability of the sperm. Applicants have not shown the criticality of all pressures of 50 psi and above and the criticality of all sampling rates of 900 sorts/second and above under the generic conditions set forth in the claims. There are no limitations recited in the claims which would indicate what critical elements, beyond those disclosed in the prior art, would allow the ordinary artisan to practice an improved method of sorting sperm and of obtaining a sorted equine sperm sample under the claimed broad ranges of sorting conditions. The claims do not recite any specific details of a flow sorting device that go beyond the teachings provided in the prior art. Rens teaches sampling rates of 500 sperm/second and 2000 sperm/second. Applicants have not established that the method of Rens does not result in sort rates of 900 viable sperm per second. If the flow cytometry device of Rens does not allow for such sort rates, it is unclear as to what type of device would allow for such sort rates. The claims do not appear to reflect any particular limitations which would distinguish the claimed sorting method over that of Rens and the claims are not limited to methods which utilize a specific, improved flow cytometry device that allows for sort rates higher than those achieved by Rens.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carla Myers whose telephone number is (571) 272-0747. The examiner can normally be reached on Monday-Thursday from 6:30 AM-5:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (571)-272-0782.

Art Unit: 1634

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Carla Myers

July 7, 2004


CARLA J. MYERS
PRIMARY EXAMINER